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A Review of Hepatico-Cerebral Disturbances.

(ABSTRACT)

INAUGURAL-DISSERTATION

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The literature on the subject of hepatico-cerebral disturbances may be divided into three periods. The first period dates from 1854 to 1898, the second period from 1899 to 1912, and the third period dates from 1912 to the present.

Frerichs in 1854 was the first to publish a case of progressive lenticular degeneration. His patient presented marked symptoms involving the central nervous system: tremor, slowness of muscular movement, dysarthria, and dysphagia. At autopsy the pathological findings in the brain and cord were insignificant. On the other hand, an extreme cirrhosis of the liver was found. During life there was a total absence of symptoms referable to the liver.

C. Westphal in 1883 reported two cases in which tremor, slowness of all muscular movement, stiffness in lower extremities, dysarthria, and dysphagia were the most conspicuous symptoms. At autopsy the pathological findings were negative. The great similarity of these two cases to those of disseminated sclerosis and the absence of pathological findings lead Westphal to apply the term « pseudosclerosis » to this condition.

In 1883 Gowers published two cases which showed striking resemblance to the case described by Frerichs. Cases were later reported by Ormerod in 1890, by Homén in 1890 and 1892, by Strümpell in 1898.

In 1899 Strümpell reported another case of pseudosclerosis. At autopsy the pathological findings in the central nervous system were negative. However, a beginning cirrhosis of the liver was observed. This seems to be the first case of those termed « pseudosclerosis » in which a liver cirrhosis was recorded. The usual symptoms of cirrhosis of the liver were absent during life.

The third period was ushered in by Wilson's work in 1912. Wilson made a very painstaking analysis of the cases recorded

by Gowers, Ormerod, Homén, and four personal observations. The symptoms developed were tremor, muscular spasticity, contractures, dysarthria, dysphagia, muscular weakness and emaciation, and various mental symptoms. The most significant pathological findings were a marked cirrhosis of the liver and a bilateral lesion of the lenticular nucleus.

In a histo-pathological study of six cases, Spielmeyer reaches the conclusion that a well defined difference between progressive lenticular degeneration and pseudosclerosis does not exist. Both diseases are but variations of the same morbid process.

In a review of the world's literature the author collected forty-four cases of progressive lenticular degeneration confirmed by autopsy. An analysis of these cases leads to the following conclusions as to symptomatology, prognosis, and pathology.

The characteristic and most constant symptoms are those involving the motor system. Tremor is always present. It is an intention tremor.

Another characteristic symptom is a change in muscle tonus. A condition of hypertonicity exists which increases with the duration of the disease. In the cases under discussion we find an extreme degree of spasticity but — and this is the most characteristic feature of the disease — all pyramidal symptoms are absent.

Contractures which form another fairly constant symptom may be divided into an early and a late stage. In the early stages the limbs assume a particular position due to the muscular hypertonicity. As a result of the prolonged contracture of this early form, myogenic changes develop and now the late stage or condition of myogenic contracture is present which cannot be overcome.

Dysarthria and dysphagia are fairly constant. The speech has been characterized from slow, monotonous, scanning, to complete anarthria. As no evidence of paralysis can be found these conditions are explained by the muscular hypertonicity.

In the great majority of cases the tendon reflexes are normal. The cutaneous reflexes are present. The sensation is almost always intact.

The mental symptoms are very variable. Conditions found were described as lethargic, emotional, apathetic, dementia, involuntary laughter, excessive irritability, idiotic.

In eighteen cases recorded after Fleischer first called attention to the corneal pigmentation, this symptom was found seven times. The corneal pigmentation involves the deepest layers and varies in color from brown to green.

Of the negative symptoms, it may be said that in uncomplicated cases the pyramidal motor system is intact. There is no impairment of sensibility. Cerebellar symptoms are absent. Nystagmus is absent.

The disease is familial, frequently attacking more than one member of a family. In fourteen of forty-four cases more than one member of a family suffered from the disease. In one case

it was father and daughter. In the remaining cases it was brothers or sisters.

Young individuals are especially predisposed. In 80% of the cases the onset occurs between the ages ten and twenty.

The prognosis is always serious. The disease steadily progresses. The symptoms gradually become worse. The condition usually ends fatally.

The pathology of Wilson's disease and pseudosclerosis is more or less characteristic. At autopsy bilateral degeneration of the lenticular nucleus is found. This degeneration varies from discoloration and sponginess through shrinkage and atrophy to complete disintegration and evacuation of the ganglion. The optic thalamus is practically always normal and the internal capsule is intact. The caudate nucleus may be somewhat atrophied. The findings in the pons, medulla, and cord are nearly always negative. In advanced cases there may be a degeneration of the ansa lenticularis, some atrophy of the corpus Lysii and degeneration of the strio-thalamic fibres.

A almost constant finding post mortem is a liver cirrhosis of unusual type. The surface of the liver is covered with irregularly rounded nodules of liver tissue of various sizes surrounded by bands of connective tissue.

Microscopically, there are great variations in the conditions of the liver cells. Side by side are seen both degenerative and regenerative processes. There are areas, showing the cells in various stages of degeneration (fatty degeneration, necrosis). Adjacent areas show the liver cells in active regeneration, judging by the presence of enlarged or double nuclei.

In the main two theories are brought forward to account for these changes in the liver:

- 1) the condition is cirrhotic in nature, the unusual form being due to the presence of regenerative processes in the liver parenchyma.

- 2) the changes in the liver are due to its rudimentary development (Hemmungsmissbildung) or to a disturbance in the organ during foetal life.

Another not infrequent pathological finding is enlargement of the spleen.

Of the pathological physiology of the symptoms involving the lenticular nucleus, our knowledge is very limited.

Mingazzini in a study of thirteen cases refers to the lenticular nucleus as a motor center. He claims that destruction of the nucleus causes a slight facial and limb paresis on the opposite side; exaggeration of the tendon reflexes on the same side; slight disturbance of sensibility, atrophy of the extremities, and anisocoria. In destruction of the posterior four-fifths of the left lenticular nucleus, dysarthria and anarthria results. If the outer third of the nucleus be involved pseudomelia parasthetica may occur.

Mills and Spiller in a study of eleven cases where lesions were restricted to the lenticular nucleus fail to find any disturbances of sensibility of motility.

Dejerine doubts the lenticular nucleus has connection with the motor or other portions of the cortex or that it plays a part in the control of movement in the function of speech. He does not believe disease of the nucleus produces definite and constant symptoms.

Dana, after a study of some cases concludes the corpus striatum has no independent or specific motor function, especially in connection with articulation.

Stieda, in a series of experiments fails to obtain motor activity by stimulation of the corpus striatum after destruction of the pyramidal motor system.

Oppenheim and Vogt after a study of some cases involving the corpus striatum, but where the internal capsule was intact recognize a syndrome of the corpus striatum consisting of tremor, spasmodic involuntary movements (athetoid), emotionalism, with little or no paralysis, sensibility remaining intact and intelligence remaining unimpaired.

Wilson says that in pure uncomplicated bilateral lesions of the lenticular nucleus, and more generally of the corpus striatum, the clinical symptoms are bilateral involuntary movements (tremor), weakness and hypertony of the musculature; dysphagia and dysarthria. Sensories remain intact. He reaches the conclusion that « the corpus striatum exercises a steady effect on the action of the corticospinal system », and that « hypertonicity or rigidity of the musculature » is « due to defect of the inhibitory action of the corpus striatum ».

The nature and pathogenesis of progressive lenticular degeneration and concurrent pathological conditions are quite obscure.

The various theories brought forward may be briefly summarized as follows:

- a) the liver elaborates a toxin which has a specific action on the lenticular nucleus,
- b) the gastro-intestinal tract may be the source of this toxin which causes the cerebral and hepatic changes,
- c) the brain may be the primary cause of all the symptoms, the liver cirrhosis secondary,
- d) the disturbance of a bile-secreting center located in the brain,
- e) hereditary syphilis may be the underlying factor,
- f) a disturbance of the glands of internal secretion may be the cause.